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Air-borne Tubercle Bacilli.—Whether tubercle bacilli are transmitted in actual droplets, droplet nuclei or dried dust particles is still a debatable question. In attempting to recover bacilli from the air in tuberculous milieux, three series of tests were run at Barlow Sanatorium: (*1*) Dishes were set out on the floors of rooms for seven days; the collected dust was processed for smear, culture and animal inoculation; a total of 26 tests were run, using 97 dishes: 7 tests in the laboratory and animal house, 19 in hospital rooms. No living tubercle bacilli were recovered. (*2*) An electric pump device was used to suck air through 2 cotton filters; 7 tests in 7 hospital rooms housing 10 patients, most of whom were strongly positive, open cases, were made; no bacilli were found in the filters. (*3*) A device for running air through a nebulized spray of sterile water was next used for an average of six hours in each of 5 rooms housing 6 patients. Again, no bacilli were found by culture and animal inoculation. These results inevitably raise many questions concerning air-borne transmission of tuberculosis. Hygienic measures employed in the Sanatorium may account in part for these negative results; inadequate facilities for obtaining live bacilli from the air, as well as technical difficulties in demonstrating the bacilli are also responsible. Because of continued infection of student nurses in spite of presumably good hygienic technique, some major means of transmission of the disease must obtain which is not controlled by our present measures.—*Air Borne Infection in Tuberculosis, C. R. Smith, J. H. Urabec & J. L. Mason, California & West. Med., Tuberc. Supp., August, 1946, 65: 10.*—(*P. Q. Edwards*)

BCG Vaccination.—Because of an apparent variability in the virulence of BCG strains, studies were undertaken at the Danish State Serum Institute to determine the cause and effects of such alterations within a given strain. Although Calmette stated that the BCG 1, distributed by the Pasteur Institute in 1927 was a *virus fixe*, many of the schoolchildren given parenteral vaccination of 0.01 mg. developed local abscesses followed by ulcerations. Since even intracutaneous vaccinations with 0.001 mg. gave rise to abscess and ulcer formation, it was apparent that the strain was too virulent for use in humans. Calmette then sent another strain, BCG 423, which proved to be much less virulent. Comparison of these two strains by inoculations of both guinea pigs and men showed that BCG 1 was much more virulent than BCG 423 not only because of an R-S dissociation phenomenon, as first described by Petroff in 1927, but also because of continued bile-potato transfer which increased the virulence of a given strain. Repeated transfer on Sauton's medium over a long period of time produced a gradual decrease in virulence due to the presence of an iron salt, ammonio-ferric citrate, which undergoes chemical change in the presence of moisture. Small amounts of copper in the distilled water also were found to affect the virulence of the vaccine. Because of this variability in the virulence of BCG vaccine, great care should be taken to determine the virulence of a given strain before use in vaccination. If the viru-

lence is too high, local abscesses and adenitis may result; whereas a virulence too low will not produce satisfactory resistance and "spontaneous" tuberculosis will appear in the vaccinated subjects. The best way to keep the vaccine at an optimal level of effectivity is by growing the BCG strain on Sauton medium and interposing some bile passages when the virulence begins to decrease. Control of the strain may be effected by intracutaneous tests on guinea pigs and by keeping accurate records of any complications developing in the vaccinated subjects. Above all, practitioners should realize that the old concept of a *virus fixe* is not applicable to the BCG strains used for vaccination.—*Practice of the Calmette Vaccination, K. A. Jensen, Acta. tuberc. Scandinav., 1946, 20: 1.*—(*P. Q. Edwards*)

BCG in Denmark.—On the basis of the experience in Denmark it is concluded that BCG vaccination is safe, that—with experienced workers—complications are relatively few, that the proper level of virulence of the BCG strain (which is *not* a *virus fixe*) must be closely watched and controlled and that this vaccination gives considerable protection, against the "morbid phenomena accompanying the tuberculous primary infection, and it also affords a considerable protection against genuine tuberculosis of the various organs—in particular, against phthisis." The number of persons vaccinated annually in Denmark increased from 82 in 1934 to 40,000 in 1945.—*BCG Vaccination in Denmark, J. Holm, Pub. Health Rep., September 6, 1946, 61: 1298.*—(*M. Pinner*)

BCG.—Vaccination with BCG confers the capacity of a specific reaction against tubercle bacilli. This is known as "tuberculous premunition." It does not result in immunity but helps to avoid the primary infection with its disseminations. In Paraguay, the mortality of tuberculosis was 20 for 10,000 population before the vaccination was started in August, 1941. A total of 97 per cent of all tested persons, 87 per cent of all children under 10 years and 95 per cent of all adolescents under 20 years were tuberculin reactors. This shows that tuberculosis in Paraguay has epidemic proportions. Since 1941, 2,388 persons were vaccinated. Of those 113 were more than 25 (up to 51) years old. Only children and adults who showed an anergy against 5 mg. of tuberculin and 1,052 babies, about one-tenth of all new-born, were vaccinated. The multiple puncture method of Rosenthal modified by Etcheverry was used. Only occasionally was BCG given orally, especially in children with eczema or dermatitis. No accidents happened. Tuberculin tests were only made in children and adults: 27 per cent turned positive on the first day, 53 per cent on the eighth day and 97 per cent one month after vaccination with BCG; this persisted in 70 per cent until the end of one year; 88 per cent of those with negative skin tests who were revaccinated showed a positive reaction at the end of the third year. The oral administration of BCG resulted in only 48 per cent reactors. In the female sex there was a distinctly higher percentage of allergy acquired by BCG. The multiple puncture method did not produce any nodules or ulcerations, which are very frequent with the intracutaneous and subcutaneous methods. Pleural, pulmonary or mediastinal changes were not observed. There was no proof that there is any relation between BCG vaccination and enlargement of hilar lymph nodes. Ninety-five per cent of the vaccinated males and 96 per cent of the females had normal X-ray films, 1 per cent showed enlargement of the hilar nodes and 3 per cent, calcifications. Of the 2,388 vaccinated, not one acquired tuberculosis. This is the more remarkable, since the expected morbidity amongst the vaccinated persons is at least 40 to 60. In the nonvaccinated anergic part of the population, the incidence of tuberculosis was 9 per cent. Amongst 200 nonvaccinated anergic persons who were examined, 10 cases (5 per cent) were found to have active pulmonary lesions, 8 (4 per cent) hilar adenopathy. Amongst the 1,857 vaccinated who have been under observation for more than one year, 4 deaths of tuberculosis could be expected. None occurred. The

authors believe that this is due to the BCG vaccination which they consider the basic method in the prophylaxis against tuberculosis.—*Posicion de la vacuna B.C.G. en la profilaxis de la tuberculosis, A. R. Gines & V. Rebull Richieri, Rev. de tuberc. d. Uruguay, April, 1945, 13: 255.*—(*W. Swienty*)

BCG.—This is the report of the Uruguayan Commission for the study of BCG vaccination in the prevention of tuberculosis, given to the Pan American Tuberculosis Congress in Havana, January, 1945. Only some of the conclusions of this thorough paper, which reviews the work done in Uruguay in this field since 1930, can be given. The oral vaccination of the new-born has been more and more abandoned in favor of the subcutaneous, the intracutaneous and the multipuncture (Rosenthal's) methods. The authors who have vaccinated over 103,000 babies do not share in an exaggerated enthusiasm for BCG vaccination. The mortality from tuberculosis amongst the vaccinated and nonvaccinated was almost the same: 7 per cent of the vaccinated and 5.2 per cent of the nonvaccinated died of tuberculosis. The authors do not believe that there is any specific immunity conveyed by the application of BCG, especially if it is not repeated. Of the 103,208 babies, 68,005 babies received BCG orally; 15,302, subcutaneously; 1,372, intracutaneously; 18,359, by the multiple puncture method; 8,000 babies are vaccinated every year which represents 20 per cent of all newborn. It was found that the intracutaneous vaccination results in early, intense and prolonged allergy. The protection obtained by BCG is most obvious where the baby continues to live in infected surroundings and is exposed to massive contact with tubercle bacilli. But, in spite of the improvement in the administration of BCG and in spite of the resulting allergy, BCG has not been able to check tuberculous infection and evolution. Despite some favorable results, the vaccinated baby should not be allowed to live in an infected medium. In fact, no baby should be vaccinated if separation from his contacts cannot be obtained. Very important is a close follow-up with control of the development of the allergy. Revaccination should be done as soon as allergy fades. BCG administered parenterally can increase or even start defenses against superinfection, but this protection is subordinated to a great many factors. The authors believe that the intracutaneous and Rosenthal's method should be used on every baby coming from tuberculous or suspicious contacts. Periodic tuberculin tests should be made and revaccination be done as long as anergy persists. The protection so obtained is only relative. It is of value against discreet infections and occasional slight exposure, whereas no protection is obtained against exposure to massive, early and repeated infections. The vaccination with BCG is still in its trial stage. The real fight against tuberculosis consists in the early separation of the tuberculous from the healthy. To do this there must be a sufficient number of sanatorium beds. Social legislation, health insurance, improvement of the living standard and abolition of illiteracy are the most important steps for the decrease of tuberculosis. The United States is cited as example. It is pointed out that here tuberculosis decreased without any BCG vaccination, by steady increase of the living standard and by improvement of social and health legislation.—*Posicion de la vacuna B.C.G. en la profilaxis de la tuberculosis, P. Cantonnet Blanch, H. Cantonnet Blanch & H. Lieutier, Rev. de tuberc. d. Uruguay, March, 1945, 13: 1.*—(*W. Swienty*)

BCG Vaccination in Indians.—Since December 1935, a total of 1,550 American Indians, aged one to twenty years, received intracutaneous vaccinations with BCG; they all did not react to tuberculin prior to vaccination. These, as well as 1,457 controls, were observed for a period of six years with yearly chest roentgenograms and tuberculin tests. Of the controls, 60 died (from all causes) and 34 of the vaccinated persons. In the control group, 28 died of tuberculosis, in the vaccinated group, 4. Including the deaths just

mentioned, the tuberculosis case rate per 1,000 person-years was 24.3 in the controls and 4.7 in the vaccinated persons. The paper contains extensive statistical analyses, not only in regard to results but also to show the similarity and comparability of the test and the control groups as to age, sex, living conditions and exposure to known sources of tubercle bacilli.—*Experience with BCG in the Control of Tuberculosis among North American Indians, J. D. Aronson & C. E. Palmer, Pub. Health Rep., June 7, 1946, 61: 802.*—(*M. Pinner*)

Immunology of Tuberculosis.—Tuberculo-anaphylaxis, tuberculo-allergy and tuberculo-immunity have been produced concurrently in one and the same animal organism and alternately separated as characteristic and apparently unrelated biological phenomena. Purified tuberculoprotein possesses high tuberculin activity, is non-toxic for normal guinea pigs, sensitizes anaphylactically but not allergically and fails to immunize against virulent tuberculous infection. Elimination of tuberculo-anaphylactic hypersensitiveness by production of non-fatal anaphylactic shock (antianaphylaxis) fails to remove or impair tuberculo-allergic hypersensitiveness. Elimination of tuberculo-allergic hypersensitiveness by sustained desensitization with tuberculin fails to remove or impair tuberculo-immunity which may be maintained in the complete absence of allergic-hypersensitiveness. Intravenous injection of lethal amounts of tuberculoprotein or tuberculin in completely desensitized iathergic-immune guinea pigs infected with virulent tubercle bacilli fails to produce allergic intoxication (crucial test of complete desensitization). Localization and destruction of virulent tubercle bacilli in reinfection is significantly more effective and complete in the desensitized iathergic-immune than in the hypersensitive allergic-immune guinea pigs. Inhibition of visceral tuberculosis following the intraperitoneal inoculation with virulent human tubercle bacilli is most effective in the completely desensitized iathergic-immune guinea pigs while much of the acquired tuberculo-immunity is dissipated in the hypersensitive allergic state. The three tuberculo-biological phenomena of anaphylaxis, allergy and immunity appear to disclose distinguishing characteristics which separate them as independent phenomena. (Author's summary)—*Concurrent Development and Subsequent Dissociation of Anaphylaxis, Allergy and Immunity in Tuberculosis, K. Birkhaug, Acta med. Scandinav., November 12, 1942, 112: 393.*—(*G. C. Leiner*)

Immunology of Tuberculosis.—Acquisition of immunity in guinea pigs is found in response to attenuated living bacilli rather than to injections of the various component parts of the organisms: polysaccharide, phosphatide, wax, protein combined with phosphatide, unheated protein, bacilli from which lipids have been removed, defatted bacilli to which individual lipids have been readded or bacilli killed by moderate heat. Some heat-labile factor in the organism, a complex rather than one chemically distinctive substance, is apparently the immunogenic agent. No hypersensitivity develops in animals injected with large numbers of bacillary bodies from which the phosphatide and wax have been removed; sensitivity develops, however, when the wax is readded to the bacilli or when isolated protein and wax mixtures are employed for injection. An anti-protein immune body is responsible for serological reactions with the whole bacilli, although no correlation exists between the occurrence of such antibody and the ability of the animal to resist infection. There is no detectable immunological factor in the blood of resistant animals, with respect to the major components of the bacillary cell. Similarly, skin reactions to protein may occur independently of acquired resistance. It is apparent from present information that the nature of resistance to tuberculosis remains enigmatic.—*A Study of the Relationship of Resistance, Allergy, Antibody and Tissue Reactivity in Tuberculosis to the Components of the Tubercle Bacillus, S. Raffel, California & West. Med., Tuberc. Supp., August, 1946, 65: 13.*—(*P. Q. Edwards*)

Immunology of Tuberculosis.—A review of the studies by the author and his collaborators on the mechanism of specific tuberculo-immunity which he summarizes as follows: "(*1*) We have verified and demonstrated the following: (*a*) a tuberculin anaphylactic hypersensitiveness exists and is produced by tuberculoproteins (tuberculin) appropriately injected. It does not appear to be of any significance in the natural picture of tuberculosis in man or animals and is mainly of academic interest; (*b*) tuberculin (tuberculoprotein) anaphylactic hypersensitiveness can be transferred passively with the blood and is passed from mother to offspring *in utero*; (*c*) tuberculo-anaphylactic shock and tuberculo-allergic shock produced by the injection of tuberculin (tuberculoprotein) present entirely different clinical and pathological manifestations and can be demonstrated in the same animal under appropriate conditions. (*2*) We believe that we have verified and demonstrated the existence of a relative specific tuberculo-immunity produced by (*a*) viable (avirulent human and bovine) tubercle bacilli, but not by (*b*) heat-killed nonviable tubercle bacilli, nor by (*c*) the filtrate from growing tubercle bacilli on a nonprotein synthetic medium nor by (*d*) tuberculoproteins (tuberculins). This specific tuberculo-immunity must be produced actively and persists over four years; it cannot be transferred passively with the blood and it does not pass from mother to offspring *in utero*. There is no means of measuring the specific immunity at present except by virulent infection. (*3*) We have verified and demonstrated the existence of a specific tuberculo-allergy which is produced by (*a*) viable tubercle bacilli and by (*b*) heat-killed nonviable tubercle bacilli which are more efficient when suspended in paraffin or mineral oils. This specific tuberculo-allergy appears to be no measure of immunity, although it may be produced during infection coincident with it. When produced by avirulent tubercle bacilli, tuberculo-allergy reaches a maximum at about two months and may disappear in about six to twelve months. It cannot be transferred passively with the blood nor is it passed from mother to offspring *in utero*. Desensitization or immunization against allergic tuberculin hypersensitiveness can be achieved by appropriate injections of tuberculin. Allergic bacillary hypersensitiveness is not affected by tuberculin injections so that tuberculin therapy appears futile for this purpose practically. Specific tuberculo-immunity and specific tuberculo-allergy play a significant though individual part in the picture of clinical tuberculosis."—*Fundamental Information on the Mechanism of Specific Tuberculo-Immunity, H. J. Corper, J. Lab. & Clin. Med., March, 1946, 31: 346.—(F. G. Petrik)*

Spread of Dye in Allergy.—The authors observed that in guinea pigs with the allergy of tuberculosis as well as with other bacterial allergies, the skin shows a marked ability to restrict the spread of vital dyes injected intracutaneously. Local fixation of injected antigens has been shown by Opie to occur as the result of antigen-antibody combination, while Menkin has emphasized the nonspecific factor of inflammation with lymphatic blockade in this phenomenon. The injection of small amounts of vital dye into the skins of allergic animals bears no obvious relationship to either concept, however, since neither a specific antigen-antibody reaction is involved nor is there apparent inflammation. The authors followed the dye limiting ability in the skin of groups of guinea pigs sensitized with BCG, with staphylococci and with horse serum. In these three instances—two of bacterial allergy and one of anaphylactic sensitivity—the limitation of spread of the dye "Pontamine Sky Blue" became evident before the appropriate tests for sensitization could be elicited. In the case of the bacterial allergies, dye limitation was apparent on the seventh day after bacterial inoculation, and in the horse serum treated animals after two days. As sensitivity increased the effect became more pronounced. Desensitization of BCG animals with tuberculin and of anaphylactic animals with horse serum caused

a loss of the epidermal dye restricting property. It is concluded that the ability to localize intracutaneously injected vital dye accompanies the anaphylactic as well as the bacterial allergic state and that specific desensitization eliminates this capacity. An explanation for this effect is difficult to supply.—*Intradermal Spread of Vital Dye in Anaphylaxis and Bacterial Allergy, K. Birkhaug & J. Böe, J. Immunol., October, 1946, 54: 107.*—(*S. Raffel*)

Tuberculin Allergy. — Typical asthmatic attacks ending fatally have been produced in experimental animals. Guinea pigs were given an intraperitoneal injection of BCG (1.5 mg.), and after several weeks were subjected to the inhalation of a 5 per cent solution of tannin-tuberculin (Schuberth). All animals subjected to the inhalation of this solution, which was dispensed as a fine mist of particles not over 0.005 mm. in diameter, developed typical severe asthmatic attacks. If the inhalation was discontinued after five minutes, the animals recovered. Prolongation of the experiment up to eight and ten minutes caused the death of all animals. At autopsy the findings were typical of those seen in bronchial asthma with acute emphysema of the lung and abundant bronchial secretions. The bronchial vessels were choked with eosinophils. A few animals showed rare tubercles in the lungs, and around these were perifocal hemorrhages. Animals surviving this experiment because of brief exposure to the solution were given 1 mg. of tannin-tuberculin intravenously. Those animals were dead within twenty-four hours of the typical findings of tuberculin-shock. The lungs did not show the characteristic picture of acute emphysema as in the first experiment. Previous administration of suitable doses of calcium subcutaneously was capable of preventing or modifying asthmatic attacks in susceptible animals. The author concludes that tuberculin allergy can be manifest in much the same way as ordinary allergies and that the mechanism is fundamentally the same when the "shock organ" is exposed to the proper antigen. There is abundant clinical evidence to support these conclusions in laboratory workers who have sustained asthmatic attacks after working with dry preparations of tuberculin.—*Weitere Beiträge über die biologischen Eigenschaften des Tuberkulins, P. Kallos, Acta med. Scandinav., June 23, 1942, 60: 493.*—(*H. Marcus*)

Hematology in Experimental Tuberculosis. —The rôle played by allergy in resistance to tuberculosis, an issue of repeated debate, is here presented from the point that allergy is not necessary for the operation of immunity in this disease. The postulation is put forth that a specific allergen and immunogen are responsible for the production of tissue inflammation and necrosis at one extreme and resistance to infection at the other and constitute the bacterial allergy and true immunity; "allergy is the shadow but not the substance of immunity in tuberculosis." The fact that guinea pigs, when primarily infected with virulent tubercle bacilli, react with variations in blood cellular ratios and formed elements with a constancy and in direct progression with advancing disease constitutes a method of determining with some accuracy the status of visceral tuberculous disease by hematological means. Out of three series of guinea pigs, those of the first group were rendered highly resistant, "iathergic immune" by subcutaneous injection of BCG vaccine. A portion of these animals were desensitized by triweekly injections of tuberculin. The injection of virulent tubercle bacilli into these three groups of animals presented the following blood changes. Hemoglobin percentages showed little variation in the desensitized animals. In the allergic group, the hemoglobin fell significantly though not to the extent as that seen in the control group. In the latter, the fall was most rapid and most excessive and fell to nearly 50 per cent of normal. The influence of virulent tuberculous infection on the red cells was similar to the effect on the hemoglobin. Desensitized animals, however,

showed almost 20 per cent increase in red blood cells; this enhanced erythropoiesis in the presence of a tuberculous infection suggests a high degree of tuberculo-resistance. Leukocytosis in the control animals showed a deviation of over 50 per cent increase; this probably represents the true picture of leukocytosis during a virulent tuberculous infection. Differential counts indicated only the slightest deviation from the base line in regard to the numbers of young metamyelocytes in any group of animals and only insignificant variations in the numbers of older metamyelocytes. Segmented cells varied only slightly in numbers in the first two groups; in the control animals, however, the increase was slight but of sufficient degree to be significant. There were no significant alterations in the numbers of circulating basophiles or eosinophiles. Desensitized animals exhibited no abnormal values for lymphocytes but in the allergic and control animals there was a decline in the numbers of circulating lymphocytes. Progressive lymphopenia is, therefore, indicative of advancing disease. The course of the disease was reflected very closely by the variations in the numbers of circulating monocytes. The most noticeable variations occurred in the allergic and control animals in which advancing monocytosis occurred during the post-inoculation period. The leucocytic index (Crawford-Medlar), which equals the value of the neutrophile-lymphocyte percentage ratio plus the value of the elevation of the monocytes plus the value of the abnormal total white count, records most accurately the trend of advancing disease; values below 15 indicate the most favorable prognosis. The monocyte-lymphocyte ratio was elevated in the allergic and control animals; though less sensitive than the Crawford-Medlar index, the monocyte-lymphocyte ratio, when elevated, signifies advancing disease. This hematological study further supports the bacteriological pathological data that immunity in tuberculosis operates at its best when the allergic hypersensitiveness has been abolished. — *Hematology in Experimental Tuberculosis, K. Birkhaug & H. Schjelderup, Acta med. Scandinav., April 17, 1943, 113: 527.*—(*E. R. Loftus*)

Tuberculosis and Trichinella.—While studying the incidence of trichinella in North Carolina, evidence was obtained suggesting than an unrelated disease process may alter the interpretation of the trichinella skin test. Since experiments conducted with patients were unsatisfactory, experimental infections in guinea pigs were produced. Group A pigs were fed trichinella larvae, group B were injected with tubercle bacilli, group C were simultaneously fed trichinella larvae and injected with tubercle bacilli and group D animals served as controls. Preliminary skin tests with tuberculin and trichinella antigen were all negative. At autopsy all animals inoculated with tubercle bacilli revealed tubercles in the tissues. Those in group A, infected with trichinae alone, had a light (one-plus) infection at autopsy. In 4 the diaphragm was positive; in 3 the diaphragm was negative, but skeletal muscles were positive for trichinae. There was no difference in the extent of the tuberculosis seen in the two groups innoculated with tubercle bacilli, but in the tuberculous animals also fed trichinae, the latter infestation was strikingly increased in most animals, parasites easily being found in the diaphragms. In some instances the infestation was up to 1,600 times as great as in the nontuberculous animals fed the same dose of larvae. An increased density of infestation with trichinae in the presence of active pulmonary tuberculosis may account for previously reported higher incidence of positive reactions to trichinella antigen in patients confined to sanatoria than in comparable groups in general hospitals.—*The Effect of Simultaneous Tuberculous Infection on Experimental Trichinella Infestations in Guinea Pigs, O. T. Travis, G. T. Harrell & E. S. King, Am. J. M. Sc., June, 1945, 209: 758.*—(*G. F. Mitchell*)

Cattle Tuberculosis in U.S.A.—When the Tuberculosis Eradication Division of the

Bureau of Animal Industry, United States Department of Agriculture, first tuberculin-tested in 1917, 3.2 per cent reactors were found. Following thirty years of systematic eradication work, 0.18 per cent reacted in 1943 and 0.23 per cent in 1946. By now, all counties and Territories of the United States are modified accredited free areas. While in 1920, 1.62 per cent of all slaughtered cattle were condemned because of tuberculosis, this percentage had dropped to 0.03 by 1938. But, because of man-power shortage during the war, some increases have occurred since 1943. The Division has also conducted a successful eradication program in fowl and swine, the latter being frequently victims of the avian type of tubercle bacillus.—*Control of Bovine Tuberculosis in the United States, (unsigned), Pub. Health Rep., September 6, 1946, 61: 1315.—(M. Pinner)*

Pleural Absorption of Dyes.—The absorption of soluble and inert substances in the pleura was studied by endopleural injections of 5 cc. of a 1 per cent solution of methylene blue. The urinary elimination of the dye was determined one hour, two hours and twenty-four hours after the injection. When the capacity of absorption of the pleura is conserved, the elimination begins early after the administration. For practical reasons it is sufficient to determine the twenty-four hour output of the dye. The test was performed only in individuals having pneumothorax or pleural effusion. It was noted that the amount of dye eliminated in the first twenty-four hours was greatest in cases with recent pneumothorax without important adhesions; in cases with adhesions, or in the presence of inflammatory pleural effusion the elimination was low. This test might become important in judging the permeability of the pleura. It is known that the removal of a certain amount of fluid, if opportunely timed, may accelerate the spontaneous absorption of the fluid. In a series of 9 cases of pleural effusion, it was seen that the elimination of the dye was parallel to the capacity of absorption of the pleura.—*Estudio sobre absorcion de colorantes a nivel de la pleura, L. G. Navarro & A. C. Roca, Rev. espan. de tuberc., December, 1945, 14: 921.—(L. Molnar)*

Agenesis of Lung.—Two cases are reported. In the first, the trachea was deviated to the right. The apex impulse was not felt anteriorly but at the base of the right lung posteriorly. Heart sounds also were heard best in this region. Roentgenographic study showed the heart and trachea to be on the right side of the chest; lung markings were seen on both sides. A lateral view showed the heart to be situated posteriorly. Bronchography revealed a relatively normal configuration on the left. There was no right main bronchus. The left upper lobe bronchus was directed anteriorly, dividing into 3 main branches which supplied both the right and left sides of the chest. Bronchoscopy failed to reveal evidence of a right bronchus. Bronchospirometric studies according to the method of Christie showed no evidence of emphysema. Intrapleural pressure readings on the left were minus 12, minus 5. Two days after this procedure the patient was found to have a pneumothorax on both sides of the chest. The findings in the other case were similar. A review of the literature reveals that the diagnosis of agenesis of a lung has been made in life only 17 times. Bronchoscopy was performed in only 10 of these cases. Alternate diagnoses are fibrosis and massive collapse. In fibrosis, there is restriction of motion on the involved side and no rotation of the mediastinum. In massive collapse, there are acute symptoms and breath sounds are diminished on the involved side. The literature contains reports of 104 cases. Of these, the author believes that only 75 are true cases. The right lung was absent in 28 and the left in 44. There was complete absence in 33 and a rudimentary lung in 35. There are many theories regarding the etiology of the condition. Anomalies of other organs have been found in association with pulmonary agenesis.—*Complete Congenital Agenesis of a Lung, J. Smart, Quart. J. Med., March, 1946, 15: 125.—(A. G. Cohen)*

Physical Diagnosis.—Ewart's sign concerns itself with physical signs in the region of the left lower lobe in patients with pericarditis or pericardial effusion. The authors have observed similar physical signs over the left lower lung in the absence of pericardial disease. Study of these cases indicates that all types of cardiac enlargement may cause these signs over the left lower lobe. The chief sign observed by the authors has been an area of dulness just below the angle of the left scapula. This sign is not always present in cardiac hypertrophy and, in some instances, the dull note could be elicited only by heavy percussion. Auscultatory changes have been prolonged expiration varying from bronchovesicular to bronchial; in some the breath sounds were diminished and moist, crepitant râles were heard. The voice sounds were sometimes altered so as to give an increased, almost nasal sound. These signs are not fixed but it is clear that variable changes from the normal occur with surprising frequency over the left base. In the group under study, every attempt was made to rule out intrinsic pulmonary disease, such as bronchiectasis, atelectasis and pneumonitis and extrapulmonary disease such as pleural effusion and elevated diaphragm. The authors believe that these signs represent a compression of the left lower lobe by an enlarged heart. Twelve case examples are summarized.—*Aids in Physical Diagnosis: Signs over the Lower Left Lung Caused Chiefly by Cardiac Enlargement, E. M. Chapman & R. G. Anderson, Ann. Int. Med., July, 1945, 23: 35.*-(*H. R. Nayer*)

Nontuberculous Lesions in Mass X-ray Surveys.—The analysis of 442,252 chest films obtained in mass surveys done by the U. S. Public Health Service revealed 4,982 cases, or 1.1 per cent, showing evidence of nontuberculous chest disease. The lesions were classified in three main categories: (1) chest abnormalities frequently resembling pulmonary tuberculosis; (2) chest abnormalities infrequently resembling pulmonary tuberculosis; (3) miscellaneous and bizarre findings. The most common abnormal findings were cardiovascular abnormalities, pneumonoconiosis, bronchiectasis, generalized fibrosis, pneumonitis, mediastinal mass, pleurisy with effusion. The high incidence of pneumonoconiosis is explained by surveys in mining regions. Although mass surveys are primarily intended for tuberculosis case-finding the accidentally found nontuberculous changes are a valuable by-product.—*Nontuberculous Lesions Found in Mass X-ray Surveys, D. M. Gould, J. A. M. A., March 31, 1945, 127: 753.*—(*H. Abeles*)

Pneumococcal Hemolysin.—The hemolytic substance produced by pneumococci also has toxic qualities and is apparently a species-specific cellular constituent. A method has been recently devised (Cohen, Halbert and Perkins) for the preparation of a concentrate of the pneumococcal hemolysin that yields material of relatively high hemolytic potency. The preparations in the present series of experiments were derived by this method from an avirulent culture of Type-II pneumococci and contained no demonstrable capsular polysaccharide. Analyses showed them to be protein in nature. The hemolytic activity of the lysin is reversibly abolished when the substance is reversibly oxidized; over-oxidization results in irreversible loss of the activity. The preparations were employed in a study of the following biological and immunological properties of the hemolysin, namely: lethal toxicity, dermotoxic activity, antigenicity and possible relation to the C-carbohydrate. Mice were used to determine lethal toxicity. A general correlation was found between the lethal toxicity and the hemolytic activity of the hemolysin. The toxic effect of the hemolysin is not necessarily due to its hemolytic effect. The heart blood of mice that died rapidly showed no gross signs of hemolysis. Reversibly oxidized hemolysin was relatively nontoxic, but when reduced with cysteine, was found toxic. Heat-treated and cholesterol-treated hemolysin were both nontoxic and lost their hemolytic activity. The intracutaneous injection of the

active hemolysin in rabbits, guinea pigs and mice resulted in local dermotoxic reactions characterized by necrosis. Heat-inactivated, cholesterol-inactivated and irreversibly oxidized hemolysin produced no necrosis; but the skin reaction with reversibly oxidized hemolysin produced the characteristic necrosis except that it was somewhat delayed. Incubation with specific antiserum generally effected a neutralization of the dermotoxic activity of the hemolysin. Absorption with rabbit erythrocytes appeared to remove the hemolytic and dermotoxic activities of the hemolysin at approximately the same relative rates. Mice immunized with the concentrate were generally capable of withstanding a subsequent injection of at least twice the LD_{50} of the hemolysin. They also exhibited a definite but low grade resistance to virulent pneumococci (Types I and II). Precipitin and precipitin-absorption tests indicated the presence of some C-carbohydrate in the hemolysin, presumably in nonantigenic form (rabbit). The combined evidence indicates that the hemolysin has the properties of a toxin and strongly suggests that its (*in vitro*) hemolytic, lethal and dermotoxic activities reside in one and the same protein component of the concentrates.—*Toxic and Immunological Properties of Pneumococcal Hemolysin, S. P. Halbert, B. Cohen & M. E. Perkins, Bull. Johns Hopkins Hosp., June, 1946, 78: 361.*—(*J. S. Woolley*)

Antibodies to Pneumococci and Polysaccharides.—In previous studies on the immunization of human beings with type-specific polysaccharides of pneumococcus the serological evidence of an immune response has been based exclusively on relative methods such as mouse protection, or the agglutination or precipitin titers of sera of the vaccinated individuals. There were no methods suitable for directly estimating the very small amount of antibody ordinarily present in human sera. Recently, however, it has been found possible to estimate the antibody nitrogen by quantitative absolute methods even when in amounts as small as a few micrograms. The present paper deals with data obtained by these new methods with the sera of a group of medical students injected with type I and type II killed pneumococci, of another group injected with small amounts of type I and type II specific polysaccharides, and of a third group injected with types I, II and V specific polysaccharides. Injections of type-specific pneumococci or equivalent amounts of their type-specific polysaccharides led to comparable antibody production. In general, the few hundreds of a milligram (0.03 to 0.06 mg.) of polysaccharides injected functioned as extraordinarily powerful antigens. One subject produced within three weeks more than 25,000 times as much circulating anti-specific polysaccharide II as the amount of the polysaccharide injected. In man the specific polysaccharides of pneumonia are the most powerful antigens known. Subcutaneous injections of the polysaccharides were as effective as intracutaneous, and the resulting antibody levels, which were highly variable individually, remained relatively constant for five to eight months, gradually tapering off during periods of observation that exceeded two years in some instances. After five months the subjects were given intracutaneous doses of 0.01 mg. each of polysaccharide I and II. The intensity, however, of the immediate and twenty-four-hour reactions bore no relation to antibody levels in the sera. It might have been expected that these tests would have acted as "booster" doses and increased the antibody level, but the next bleeding, two, one half to four weeks later, showed no such effect, nor was there any increase in the average values for the entire group even after two years. It is difficult to assign a reason for this failure. The specific polysaccharides of pneumococcus are resistant to the usual carbohydrate-splitting enzymes. It is therefore possible that these antigens enter into a long lasting combination with some cellular constituent, and that this combination provides the observed antigenic stimulus over the comparatively long period of observation to which the groups of students were subjected. If,

at any period, the body should make its maximum response to the residual antigen available, injection of a further small quantity would not necessarily increase an already maximal effort at the production of antibody, even though the current level were below the original. One would not then expect reinjections of polysaccharide to exert much effect until all residues of previous injections had disappeared, and this state would be indicated by the disappearance of the antibody. Possibly, because they frequently harbor pneumococci, normal human beings appear to be in serological equilibrium with the C-antigen of pneumococcus, and in most instances the quite appreciable anti-C content of their sera remained relatively constant during periods of a year or longer. The so-called C-antigen is a somatic antigen common to all pneumococci. Many of the sera also contained antibody to specific polysaccharide VII.—*Antibody Formation in Volunteers following Injection of Pneumococci or Their Type-Specfic Polysaccharides, M. Heidelberger, C. M. MacLeod, S. J. Kaiser & B. Robinson, J. Exper. Med., April, 1946, 83: 303.*—(*J. S. Woolley*)

Antibodies against Pneumococci.—The antipneumococcic mouse-protective activity of sera from human subjects before and after inoculation with pneumococci or type-specific polysaccharides was measured in this study and compared with the amount of precipitable antibody nitrogen in the same sera. The measurements of this nitrogen are reported in the preceding abstract (J. Exper. Med., April 1, 1946, 83: 303). With the mouse protection tests the *in vivo* potency of the antibodies can be compared with *in vitro* evidence of their presence and activity. The protection tests were carried out in the Laboratories of the New York City Health Department using the Department's standard methods. Twenty-seven samples from 12 subjects were tested for type I protection and 31 samples from 14 subjects for type II protection. The sera studied were representative samples from the immunized subjects whose antibody nitrogen had already been determined. Because of insufficient amounts of serum only part of the mouse protection tests were carried out with the full number of mice and with repetitions of the tests as prescribed for the titration of therapeutic sera. Agreement with the antibody nitrogen method was good in the findings with hyperimmune (rabbit) sera examined repeatedly and in the human sera in which determinations were repeated using 10 mice per dilution. The ratio, mouse-protective units to antibody nitrogen, was less in human sera of low potency than in more potent animal or human sera.—*Mouse-Protective Titers of Sera of Volunteers following Injection of Pneumococci or Their Type-Specific Polysaccharides, A. M. Walter, E. L. Schenkein & W. D. Sutliff, J. Exper. Med., April, 1946, 83: 321.*—(*J. S. Woolley*)

Pneumonia.—Forty-five patients with pneumococcic pneumonia were treated by the oral administration of penicillin. The treatment was started in the majority of patients within forty-eight hours of the onset of symptoms. The usual dosage consisted in the initial administration of 200,000 units followed by 50,000 units every two hours. After the crisis no penicillin was administered during the night. With few exceptions the duration of treatment varied from four to seven days. There was no reaction to the drug except the appearance of an urticarial rash in one patient. There was one death in this series occurring six hours after admission. One patient developed empyema. Eight patients developed small pleural effusions which resorbed spontaneously. Eight patients showed delayed resolution of the pneumonic infiltration. Thirty-six patients developed an abrupt crisis, that is an abrupt fall in temperature with accompanying signs of amelioration of the infection in the absence of peripheral failure. Twelve of the 36 patients showed a secondary rise in temperature during the second or third day of therapy, 5 patients at a two to five-day interval after the cessation of therapy.—*The Treatment of*

Pneumococcic Pneumonia with Orally Administered Penicillin, P. A. Bunn, W. McDermott, Susan J. Hadley & Anne C. Carter, J. A. M. A., September 29, 1945, 129: 320.—(H. Abeles)

Pneumonia.—A study of the results obtained in 100 cases of pneumococcic pneumonia in soldiers treated with sulfadiazine and 75 treated with penicillin revealed that the response in the two groups was almost identical, the only differences being a more abrupt fall in the temperature and fewer instances of extension to another lobe during therapy with penicillin. In studies designed to determine the minimal effective therapeutic dose of penicillin, 10,000 units four times daily for three days intramuscularly produced clinical cures in every instance, but with smaller doses there were relapses and failures to respond to treatment. The clinical course of 40 patients with moderately severe primary atypical pneumonia, as compared with 40 controls, was not altered by treatment with penicillin. Of 20 patients with pneumococcic pneumonia treated with penicillin-beeswax-peanut oil mixture, 12 made an uneventful recovery following six injections of 100,000 units (1 cc.) given over a four-day period. Of the other 8 who received four injections of 100,000 units (1 cc. daily) over a four-day period, 4 made an uneventful recovery, one failed to respond to treatment and in 3 there were clinical relapses when treatment was discontinued. (Authors' Summary)—*The Treatment of Pneumonia with Sulfonamides and Penicillin, J. M. Kinsman, W. B. Daniels, S. Cohen, J. P. McCracken, C. A. D'Alonso, S. P. Martin & W. M. M. Kirby, J. A. M. A., August 25, 1945, 128: 1219.—(H. Abeles)*

Pneumonia in Aged.—One hundred and sixty-six cases of pneumonia in men and women 60 years of age and older have been studied. Of these, 33 cases, or 20 per cent, were fatal. Included in the series are 65 cases due to various types of pneumococci, of which 8 terminated fatally, or 12 per cent. Sulfonamide therapy was used in 128 cases. Additional type-specific serum was given in 5 of these cases. Penicillin was used successfully in 11 cases, including an empyema due to type-III pneumococci in a man aged 84 years and a meningitis due to type-II pneumococci in a man aged 74 years. Although the fatality has been dramatically reduced by recent advances in therapy, pneumonia is still a disease with high incidence and high mortality in the aged. With the proper appreciation of the complex problems encountered in the old, and with better methods of treatment, one may look for further improvement in the results. The disease appears in unusual forms both in its onset and in its course in the aged, and is commonly associated with other conditions which may obscure and aggravate it. Physicians should be on the alert for pneumonia in the aged, recognize it when it is present and treat it actively in spite of what may appear to be overwhelming obstacles. Its occurrence should not be assumed merely because of its prevalence in the aged or because of the presence of a few râles at the bases of the lungs. The period of medical development is past when an unqualified diagnosis of pneumonia on the death certificate of an elderly person was considered adequate because no one expected old persons to recover from the disease. (Authors' summary)—*Pneumonia in the Aged: An Analysis of One Hundred Sixty-Six Cases of Its Occurrence in Patients Sixty Years Old and Over, F. D. Zeman & K. Wallach, Arch. Int. Med., June, 1946, 77: 678.—(G. C. Leiner)*

Penicillin Inhalation in Pneumonia.—Twenty-five patients with pneumonia were treated with aerosol penicillin. It was found that lobar pneumonia responds less well than bronchopneumonia or bronchiolitis. The reason undoubtedly is failure of the aerosol to enter a lobe which is entirely filled with exsudate. Patients were treated with one hour aerolization therapy twice daily, 200,000 units being used for each treatment. The temperature dropped to normal by crisis

frequently after the first treatment, and penicillin therapy is continued for twenty-four hours longer. It is felt that when fever has not disappeared within thirty-six hours, the method must be judged a failure, and other forms of treatment should be instituted. Although only between 20 and 50 per cent of the nebulized penicillin is deposited in the lung, the total dose of penicillin used by this method, between 600,000 and 800,000 units, is no greater than is used by intramuscular injection in the treatment of pneumonias. This method of treatment is greatly preferred by patients to injections recurring at three-hour intervals. This treatment is not applicable to all patients. Coma and delirium are obvious contraindications, and marked pain on respiration may render the treatment unpleasant. In the series of bronchopneumonias, the only failures were those ascribable to penicillin resistance of the organisms involved.—*Pneumonie-behandlung mit Penicillin-Aerosol, P. Geiser, K. Schaub & H. Staub, Schweiz. med. Wchnschr., April 6, 1946, 76: 285.*—(*H. Marcus*)

Electrocardiogram in Pneumonia.—Four hundred and thirty electrocardiograms were made on 82 patients who survived pneumococcus pneumonia, and 19 electrocardiagrams were made on 10 patients who died of pneumococcus pneumonia. Changes in the T-waves were noted on admission in 35 of the 82 patients (42.7 per cent) who survived and in 5 of the 10 who died. In 12 patients the T-wave changes persisted after recovery. The electrocardiographic changes were independent of the type of therapy. They occurred most frequently in young patients. Postmortem examination of the hearts of 9 patients, 4 of whom had shown electrocardiographic changes, revealed no significant structural abnormality. Arterial oxygen-saturation and carbon dioxide content did not show a significant difference between patients with and without electrocardiographic changes. There was no correlation between the electrographic changes and bacteremia, location of lung lesion, presence or absence of pleural fluid, chest pain, duration of disease or fever. There was no correlation between increased plasma volume and electrocardiographic changes. Electrocardiographic changes, when due to pneumonia, have no serious prognostic importance in adequately treated patients.—*Electrocardiographic Studies during and after Pneumococcus Pneumonia, K. J. Thomson, D. D. Rutstein, D. M. Tolmach & W. H. Walker, Am. Heart J., May, 1946, 31: 565.*—(*G. C. Leiner*)

Influenza Pneumonia.—Three patients with pulmonary infections due to *Hemophilus influenzae*, type B, were treated with streptomycin. The first patient had an acute, bilateral, suppurative pneumonia, possibly superimposed on a preëxisting bronchiectasis. He showed rapid improvement following intrabronchial and intramuscular administration of streptomycin. The second patient had an acute pneumonitis superimposed on bronchiectasis. The third patient developed a persistent influenza bacillus infection of the left upper lobe following removal of the left lower lobe. These patients were treated by intrabronchial administration of streptomycin alone. They showed good response to the treatment and they recovered completely.—*Streptomycin Therapy in Hemophilus Influenzae Pulmonary Infections, T. M. Durant, A. J. Sokalchuk, C. M. Norris & C. L. Brown, J. A. M. A., May 18, 1946, 131: 194.*—(*H. Abeles*)

Endemic Pneumonia of Albino Rat.—White rats are prone to suffer from progressive bronchopneumonia ultimately resulting in purulent cavitation (bronchiectasis). This disease appears to occur naturally in older rats, immature animals being singularly free of the disease. Moreover, the rat itself is subject to a second and distinct respiratory disease, infectious catarrh, which may result in pneumonia although it more commonly affects the nasal passages and the middle ears. For the purposes of experimental study it seemed desirable to attempt the transmission of endemic rat pneumonia to some other host

in which it did not occur as a natural disease. A specific disease entity was established in a special strain of white mice by the nasal instillation of lung and exudate suspensions from each of 14 adult albino rats affected with endemic pneumonia, but free from infectious catarrh. The induced disease was characterized by pneumonia (in 96 per cent), otitis media (in 94 per cent) and rhinitis (in 30 per cent). It progressed slowly after an incubation period of seven to fourteen days and was attended by a variable mortality which reached 33 per cent in twenty-two weeks. Maintenance of the disease was regularly accomplished by direct transmission from mouse to mouse but only by the nasal route and only from the three foci of infection mentioned above. It was also transmissible by direct contact but required a prolonged period of exposure. The pneumonia in mice resembled that of the rat in its initial involvement of the bronchioles but differs in not progressing to bronchiectasis. Symptomatically and pathologically the mouse disease closely resembles infectious catarrh to which both the rat and the mouse are naturally subject. The two diseases can be readily differentiated in the mouse by microscopic examination. The disease established in mice by transfer from the rat is essentially pneumonotropic, being limited to the respiratory tract including the associated middle ears. Endemic pneumonia of the albino rat is commonly regarded as an infectious disease but its etiology is still uncertain. Critical study of endemic rat pneumonia has been particularly handicapped by the lack of suitable (disease-free) rats, the disease being universally distributed in so far as is known. An additional source of error has been the coexistence of infectious catarrh which may simulate endemic pneumonia in its initial involvement of the lung. With the development of a specially selected (bred) strain of rats, infectious catarrh was eliminated, but still a high rate of endemic pneumonia persisted in adult animals. It was for this reason that an alternative host was sought, under normal conditions free from this disease. Coccobacilliform bodies, pleuropneumonia-like organisms or other cultivable pathogenic bacteria could not be demonstrated in lung and exudate suspensions from selected adult rats, naturally infected with endemic pneumonia, or from experimentally infected mice. In view of this, experiments were carried out to determine whether the infective agent had the characteristics of a virus. The agent from mice was found active through a dilution of 10^{-7}. It failed to pass through Berkefeld N filters but was generally present in V filtrates with a loss in titer up to a 1000-fold. It was largely removed from suspension on centrifugation at a speed of 9,000 R.P.M. for thirty minutes. The sediment thus obtained showed no morphological units on ordinary staining but when impregnated with silver by the Morosow method the films did show intensely black and sharply outlined spherical particles which were smaller than the elementary bodies of vaccinia. The sediments were not sufficiently pure to warrant identification of these particles. Attempts to cultivate the agent in embryonated eggs were uniformly unsuccessful. In fluid suspension it failed to withstand storage at 40° C. for a week but remained viable for at least three months in a frozen state under dry ice. The agent thus exhibits many of the characteristics of a virus and is apparently the specific cause of the experimentally produced mouse disease. However, the agent has not been completely identified as the sole cause of the rat disease. It can be concluded that it is a frequent resident of the lung in rat endemic pneumonia.—*Studies on Endemic Pneumonia of the Albino Rat: I. The Transmission of a Communicable Disease to Mice from Naturally Infected Rats. II. The Nature of the Causal Agent in Experimentally Infected Mice, J. B. Nelson, J. Exper. Med., July, 1946, 84: 7 and 15.*—(*J. S. Woolley*)

Primary Atypical Pneumonia.—The authors present a clinical study of 75 cases and a radiographic study of 135 cases of primary atypical pneumonia, etiology unknown. A filtrable virus has been postulated in this

disease but results remain inconclusive. The apparent current increase is primarily due to the widespread use of X-rays. Three of the patients in this series were discovered only in routine X-ray examination. The incidence is high in young adults. Forty-seven per cent of this group manifested the typical syndrome characterized by a history of a cold for three to ten days followed by sudden chills, fever, dyspnea, cough, sore throat, headache and malaise. Forty per cent complained chiefly of sharp chest pain aggravated by cough and deep inspiration. Nine per cent gave only a history of about one to two weeks duration, of a chest cold and moderate cough. Four per cent had no previous history of respiratory infection and were picked up on routine physical examination. Temperature varied from normal to a maximum of 105.6° F. The fever subsided in two to five days by lysis. Pulse rate corresponded to temperature level. Asthmatic features were observed in about 25 per cent of patients, occurring commonly when resolution began. The extent of the lesion disclosed by X-rays was usually greater than that anticipated by physical examination. The fundamental pathological lesion is an interstitial pneumonitis. The main process is located about the bronchioles. The lesions are essentially similar to those found in influenzal pneumonitis uncomplicated by secondary bacterial invasion. The X-ray findings can be described as benign circumscribed pneumonia and disseminated focal pneumonia. The benign circumscribed type is fairly well localized but not sharply defined. It is of uniform density and usually located in the lower lobes. The disseminated type produces a picture of diffuse, coarse mottlings, the foci varying from 2 to 5 mm. These lesions are segmental lobular and very few show a lobar distribution. Early in atypical pneumonia, on the chest X-ray film, the transparent black lobules are surrounded by grey thickened perilobular septa. As the septa further thicken, the lobules disappear, either due to collapse or exudate, thus leading to the picture of consolidation. Resolution is manifested by irregular thinning of the septa thus enabling air to be seen again in the lobules. The time of resolution varied from six days to six weeks. There were 9 cases, 7 per cent, of the disseminated focal type. Nine patients developed slight pleural effusion, one a moderate pleural effusion and 3 developed solitary lung abscesses which healed spontaneously. In 70 per cent, productive cough began only with the onset of resolution. Sputum was usually muco-purulent although 7 patients had blood-streaked sputum. The leucocyte count was usually essentially normal. Cold agglutinins, studied in 12 patients, were present in low titre in 8, in high titre in 2 and absent in 2. Treatment was symptomatic with liberal use of oxygen where indicated. Where there is evidence of secondary bacterial invasion, pencillin and sulfonamides are indicated. No deaths occurred among these patients.—*The Clinical and Roentgenographic Manifestations of Primary Atypical Pneumonia, Etiology Unknown, J. B. McDonald & B. Ehrenpreis, Ann. Int. Med., February, 1946, 24: 153.*—(*H. R. Nayer*)

Penicillin Inhalation in Pulmonary Diseases.—Studies of the sputum of patients receiving penicillin intramuscularly showed significant amounts in cases of pneumonia, but not in chronic bronchitis, lung abscess or bronchiectasis. Patients with these diseases who received nebulized penicillin by inhalation showed significant amounts in the sputum up to eight hours after the treatment and also showed good blood concentrations. Postural drainage was given for fifteen minutes prior to the treatment. If spasm was present, an antispasmodic was given. A penicillin solution of 10,000 units per cc. was used. Treatment was given for fifteen minutes every four hours and for thirty minutes prior to retiring. A total of 80 patients were treated; most of these had already received sulfonamide drugs and intramuscular penicillin. A rapid disappearance of gram positive cocci and a correspondingly rapid appearance of coliform bacilli were noted. There was no effect upon

B. pyocyaneus, *B. proteus* or *H. influenzae*. The treatment was particularly valuable in cases of (1) chronic bronchitis with spasm and (2) congestive cardiac failure aggravated by respiratory infection. It produced dramatic subsidence of the toxemia in acute bronchitis, but was not particularly helpful in acute lung abcess. It hastened the recovery of pneumonia patients with intractable bronchitis. Tuberculosis patients with superimposed nontuberculous bronchitis were relieved greatly. Most patients with bronchiectasis were benefited but expectoration was not abolished.—*Penicillin Inhalation in Pulmonary Disease, J. H. Humphrey & H. Joules, Lancet, August 17, 1946, 2: 221.—(A. G. Cohen)*

Streptococcus Pneumonia.—In this case report of 4 patients with non-hemolytic streptococcus pneumonia, the striking features were lack of response to sulfa drugs, relative leukopenia, remissions and exacerbations of the disease with final slow resolution, frequency of joint complications and an eventual favorable prognosis. In all 4 cases alpha streptococci were isolated from the sputum in pure culture, and in one case there was associated a septicemia with isolation of the same organisms from the blood and the pleural fluid. Recovery was slow but was eventually complete.—*Streptococcal Pneumonia, J. Eriksson, Acta med. Scandinav., March 30, 1946, 124: 126.—(H. Marcus)*

Rheumatic Pneumonitis.—A 19-year old man was seen who following scarlet fever developed pain and swelling of one hip and both ankles, shortness of breath, slight generalized edema. He died in respiratory distress thirty days after the onset of acute pharyngitis and fifteen days after the onset of rheumatic pain. Microscopic examination of the lungs showed: "Few alveoli contained air. Many of them were filled with homogeneous material characteristic of edema fluid, and most of them contained cells also. Many of the cells were large mononuclear cells of phagocytic type. . . . In some alveoli were desquamated chains of septal cells, mixed in places with amorphous debris. In many places there was a thick eosinophilic hyaline membrane along the periphery of alveolar ducts, seemingly fixed as a lining to the wall, often partially surrounding an air pocket. In many places there were numerous erythrocytes free in the alveoli, indicating recent capillary hemorrhage, but in no place was this hemorrhage dense over a large area. Mononuclear cells predominated in the exudate. Mingled with them were varying numbers of polymorphonuclear leukocytes, usually sparse, nowhere heavy. Capillaries were engorged. Alveolar walls contained many mononuclear cells, some recognizable as lymphocytes and many as swollen endothelial or other large mononuclear cells. In some places there were small but dense collections of lymphocytes and plasma cells. There were strands of fibrinous material extending from some alveolar walls into the spaces. Interstitial edema was particularly noticeable in larger septa, and here also there were many focal infiltrations of lymphocytes and plasma cells, sometimes with a few histiocytes and leukocytes. Although rarely a giant cell with hyperchromatic and irregular nucleus was encountered, nothing resembling a true Aschoff nodule was found. No organisms were identified with the MacCallum—Goodpasture stain." In addition, hemorrhagic nephritis was found. There was no cardiac involvement. It is believed that rheumatic pneumonitis occurs more often than it is suspected; it is apparently sometimes mistaken for virus infection of the lungs. Physical and roentgenological signs as well as the anatomical findings of primary atypical pneumonia are similar to those in pneumonia occurring as a nonsuppurative sequel to hemolytic streptococcus infection. In rheumatic pneumonitis there may be other nonsuppurative lesions, such as arthritis, hematuria, epistaxis, purpura, erythema marginatum, encephalitis, cardiac changes. In primary atypical pneumonia there may be a high titer of cold agglutinins in the serum; in acute rheumatic fever there may be a

rise of antifibrinolysin and antistreptolysin in the blood.—*Nonsuppurative Poststreptococcic (Rheumatic) Pneumonitis: Pathologic Anatomy and Clinical Differentiation from Primary Atypical Pneumonia, C. R. Jensen, Arch. Int. Med., March, 1946, 77: 237.*—(*G. C. Leiner*)

Penicillin in Chronic Pulmonary Infections.—Forty-five patients with bronchiectasis were treated with intramuscular injections of 25,000 units of penicillin every three hours for one to two months. The treatment was of definite value during the recurrent pneumonic episodes. During the interval stages the amount of sepsis and toxemia was decreased. One-third of the patients noticed no improvement; patients with advanced bronchiectasis obtained no benefit. Seventeen patients with chronic lung abscess were treated with intramuscular penicillin. One patient healed completely, all other patients needed surgical drainage. Six patients with suppurative pneumonitis showed symptomatic improvement and decrease of toxemia. All patients needed surgical drainage. Two patients with coccidioidomycosis and one patient with *Monilia albicans* infection experienced no benefit from intramuscular penicillin treatment. Two patients with actinomycosis showed symptomatic improvement which was most marked when penicillin was used in combination with sulfonamides. Both patients were apparently cured by pulmonary resection in combination with chemotherapy. Nineteen patients with chronic bronchitis showed dramatic improvement following intratracheal administration of penicillin.—*Penicillin in the Treatment of Chronic Infections of the Lungs and Bronchi: An Analysis of Ninety-three Cases, E. B. Kay & R. H. Meade, Jr., J. A. M. A., September 15, 1945, 129: 200.*—(*H. Abeles*)

Pneumonic Plague.—A physician engaged in research contracted pneumonic plague. The correct diagnosis was made within twenty-six hours after onset of the disease. The patient was placed in an oxygen tent and sulfadiazine therapy was instituted at once. The temperature became normal by lysis and the patient recovered completely. The patient had received a large amount of plague vaccine a year previous to the illness. This is one of the very rare cases of recovery from proved plague pneumonia.—*Pneumonic Plague, E. J. Munter, J. A. M. A., May 26, 1945, 128: 281.*—(*H. Abeles*)

Lung Abscess.—Four patients with lung abscesses were treated with the long continued administration of penicillin. All patients had mixed infections. Three patients had acute pulmonary suppuration with cavity formation. Two patients recovered completely, the third one was left with a thin walled cavity as demonstrated by a bronchogram. One patient had multiple chronic lung abscesses in the right upper lobe. He received over 6,000,000 units of penicillin over a period of seven and one half months. The original abscesses cleared completely but a bronchogram revealed many saccular bronchiectatic cavities in the right middle and lower lobes.—*The Treatment of Lung Abscesses with Penicillin, C. J. Smyth & T. H. Billingslea, J. A. M. A., December 8, 1945, 129: 1005.*—(*H. Abeles*)

Loeffler's Syndrome.—In 1932 Loeffler first described his syndrome and by 1936, he had reported 51 cases, all from Switzerland. Cases have since been reported from all over the world. No uniform etiology has been demonstrated. A parasitic etiology must be considered in view of numerous cases, mainly in children, in whom eosinophilia and transient pulmonary infiltrations were accompanied by intestinal parasites—amebae, trichinae and ascaris. An allergic etiology must also receive serious consideration since some of the reported cases have been associated with asthma and vasomotor rhinitis. Engel of Shanghai first pointed out a definite association with allergy. Over a period of years he noted that a large portion of the population was stricken with a peculiar bronchitis each

May and June. This disease was called by the laity "privet cough" because of the species of *ligustrum* which flowers at that season. The symptoms consisted of a moderate cough productive of scanty sputum with a metallic taste. The symptoms lasted over two days. Engel himself suffered from these symptoms. He had X-ray films which revealed massive pulmonary consolidation which cleared in one day on one occasion and in six days on another occasion. He ran an eosinophilia of 25 per cent. He chose a friend at random who had a similar cough and whose X-ray films were similar, clearing in seven days. Two-thirds of Engel's cases were males, mostly adults. The marked seasonal incidence and epidemic form suggest a possible infectious etiology such as an atypical viral infection. Autopsy material is rare because of the benign course. Some authors believe that the lung changes are due to emboli, infarcts, bronchial asthma or atelectasis. According to Engel there is a localized allergic edema. Von Myenburg states that there is an eosinophilic pneumonia. He bases this on examinations in 14 accidental deaths. The symptoms consisted of low-grade fever, some cough with expectoration, a metallic taste occasionally noted in the sputum, occasional mild chest pain and asthmatic breathing. On the whole the condition is discovered on routine examination. Twenty-five per cent are discovered accidentally. A more acute form is described which persists longer. A chronic mild form is also described, but it is not certain that these three types are varieties of the same thing. Pleural effusion and asthma occasionally complicate the picture. The signs are few, but dulness on percussion, diminished breath sounds and a few migratory râles are sometimes noted. The white count usually ranges between 8,000 and 15,000 with an eosinophilia. The X-ray films reveal large irregularly outlined infiltrations, unilateral or bilateral, or small infraclavicular infiltrations comparable to those described by Assmann. A suddenly appearing consolidation which disappears rapidly over a two-week period leaving fine scars is truly characteristic. Other consolidations may appear in other areas. The differential diagnosis lies between tuberculosis, embolus with infarction, pneumonia, asthma with partial atelectasis, erythema nodosum and viral infection. The prognosis is good. There is no special therapy unless parasites are found in which case the parasitic infestation requires treatment. A case history is presented.—*Loeffler's Syndrome (Transient Pulmonary Infiltrations with Eosinophilia), H. I. Spector, Dis. of Chest, September-October, 1945, 11: 380.*—(*K. R. Boucot*)

Loeffler's Syndrome.—Fifteen patients with creeping eruption, a skin lesion usually caused by *Ankylostomum braziliense*, were X-rayed at intervals of three days for at least fourteen days. In 9 patients transient, migratory, pulmonary infiltrations were found. The pulmonary lesions appeared usually after the seventh day of the skin invasion. All patients had peripheral eosinophilia. Sputum eosinophilia varied from 2 per cent to 90 per cent. There was a paucity of pulmonary symptoms and clinical signs.—*Loeffler's Syndrome Associated with Creeping Eruption (Cutaneous Helminthiasis), D. O. Wright & E. M. Gold, J. A. M. A., August 11, 1945, 128: 1082.*—(*H. Abeles*)

Loeffler's Syndrome.—Most cases of Loeffler's syndrome have rather mild symptoms, such as general malaise, low-grade intermittent fever and upper respiratory symptoms. Laboratory findings are eosinophilia, slightly increased sedimentation rate and a normal or slightly elevated leukocyte count. X-ray findings, often discovered on a routine chest film and confirmed by subsequent films, are transitory pulmonary densities varying considerably in size and contour. There is no characteristic distribution and they may be unilateral or bilateral. The individual lesions are usually sharply demarcated, with irregular hazy borders. The density may be homogeneous or mottled and the process may extend in various directions to involve the greater portion of one or more lobes. Similar

shadows may appear in any part of the lungs and recurrences extend over a period of months. The initial lesion may be mistaken for tuberculosis, pneumonia, atypical pneumonitis, fungus infection, et cetera. Loeffler thought that the pulmonary manifestations in most of his cases were on an allergic basis. Others have reported various parasites producing transient pulmonary infiltrations, and some have reported such lesions associated with definite asthma. Apparently many and varied agents may produce this allergic pulmonary response, due to the mild nature of the disease postmortem examinations are infrequent. A case is reported which the author feels justified in classifying as one of Loefflers' syndrome. Since the pulmonary shadows are generally due to a secondary allergic response it is permissible to compare them with the "id" reaction of the dermatologist and it is suggested that the pulmonary manifestation be a "pneumonid."—*Transient Successive Pulmonary Infiltrations, M. Eichwald & W. V. Singletary, Radiology, March, 1946, 46: 258.*—(*G. F. Mitchell*)

Tropical Eosinophilia.—Eosinophilic lung often occurs in India and is known to develop in Europeans so that it may also involve Americans returning from the Orient. The disease was described in 1940 by Frimodt-Möller and Barton as a pseudo-tuberculous condition associated with eosinophilia and 175 cases were reported from a tuberculosis sanatorium in South India. Roentgenograms were described as showing "evenly distributed extensive mottling of small nodular shadows over both lung fields with increased linear markings". It was felt, after careful study, that the syndrome was not explainable on a basis of any known clinical entity. No definite etiology is known. Weingarten believes that climatic and geographic factors are important, while the asthmatic manifestations of the disease and eosinophilia suggest an allergic factor. Others attribute the disease to the Cheese-mite. There is no seasonal incidence, and age, race, social status and eating habits are not apparent factors. It may eventually be related to the syndrome described by Loeffler. The onset is characterized by lassitude, anorexia and fever of 100 to 101° F. in the evening. A dry hacking cough develops which is usually worse at night during the second week of illness. The cough becomes more severe and paroxysmal and is accompanied by wheezing and expiratory dyspnea simulating asthmatic bronchitis. Occasionally a sudden asthmatic attack may usher in the disease. Those in whom distress is greatest during the night may be relatively comfortable during the day. After a few weeks the fever and weakness subside and weight loss ceases, but the bronchopulmonary symptoms persist and become chronic unless treatment is instituted. In a few cases fever and bronchopulmonary symptoms are not significant. In mild cases physical examination reveals slight hyperresonance, prolongation of the expiratory sounds and sibilant and sonorous rhonchi with occasional crepitant râles at the bases. In more severe cases the physical findings are those of a true bronchial asthma. The sputum is usually scant, glassy, tenacious and often contains clumps of eosinophils with only occasionally a Charcot-Leyden crystal or Curschmann spiral. The spleen which is enlarged 3 to 5 cm. below the costal margin during the febrile period, is usually smooth, firm and not tender. A massive eosinophilia is present, the total white count usually being above 20,000 and often above 40,000. In some instances a count of 70,000 to 80,000 is obtained. This elevation is essentially due to an increase in the number of the eosinophils which may be 92 per cent of the total white cells. Weingarten believes the eosinophils are mature and normal, but Simeons states that their nuclei are abnormally lobulated. A mild secondary anemia may be present, and the sedimentation rate moderately increased. Blood chemistry, urine and stools reveal nothing of significance. Roengtenograms obtained at the end of the second week reveal a distinct mottling throughout both lung fields. The individual lesions varying from 2 to 5 cm. in diameter have a denser centre

and a poorly defined, blurred periphery. The areas of mottling are larger and more numerous in the hilar region and occur more frequently in the bases than in the apices. The early stage of the disease, characterized by this diffuse pulmonary mottling, seldom lasts more than four weeks and then gradually disappears leaving only prominent hilar and truncal markings. In a few cases no pulmonary abnormality can be demonstrated. The very effective treatment, discovered by chance, is neoarsphenamine, usually given every fourth day in a course of six treatments. At first there is a slight increase in the total white count, but later it abruptly drops. Clinical symptoms completely and rapidly disappear after the third injection. While there is nothing pathognomonic in the chest film and the disease may mimic other bronchopulmonary conditions, the diagnosis is not difficult, but it is important because the treatment is simple and effective.—*Eosinophilic Lung, P. J. Hodes & F. C. Wood, Am. J. M. Sc., September, 1945, 210: 288.—(G. F. Mitchell)*

Tropical Eosinophilia.—The findings in 8 cases of tropical eosinophilia are analyzed. The disease as originally described is characterized by cough, fever, weight loss, hemoptysis, asthma (or bronchitis), leukocytosis, eosinophilia and an X-ray picture closely resembling that of miliary tuberculosis. All but one of the author's cases were under 30 years of age and 6 of them were males. A low, irregular fever lasted several weeks and was accompanied by dry cough. Physical signs over the chest were variable and transient. Many small scattered foci and prominent hilar shadows were seen in the chest film. Enlargement of the spleen was present in only 2 patients. Four patients had enlarged inguinal lymph nodes. The white cell count ranged from 15,000 to 25,000, the eosinophils, most of which were mature, from 32 to 67.5 per cent. The blood changes may persist long after the acute symptoms have subsided, sometimes for years. In no case was anemia found; the sedimentation rate was increased. Wassermann and Kahn tests were done in 7 cases, in 4 of which the former was positive and the latter negative; there was no evidence of syphilis in these cases. As for treatment, various arsenicals were used, the efficacy of which remains doubtful. However, the prognosis is generally good and most patients recover without treatment. The etiology is unknown; allergy seems unlikely, in view of the clinical picture and the increased sedimentation rate, which are more in favor of an infectious origin.—*Tropical Eosinophilia, I. G. K. Menon, Indian M. Gaz., January, 1945, 80: 24.—(P. Lowy)*

Experimental Loeffler's Syndrome.—Intratracheal instillations of horse serum in sensitized rabbits caused transitory pulmonary infiltrations which were roentgenologically demonstrable and which cleared within one to two weeks. The lungs showed congestion, edema and eosinophilic infiltrations of the tracheal and bronchial mucosa and of the parenchyma, as well as areas of atelectasis and emphysema. However, in contradistinction to the disease in man, the pulmonary lesions were not migratory and there was no eosinophilia in the peripheral blood. [The similarity between Loeffler's syndrome and the experimentally produced lesions does not appear to be essential.]—*Transitory Pulmonary Infiltrations (Loeffler's Syndrome) in Rabbits, P. A. Herbut & F. R. Kinsey, Arch. Path., May, 1946, 41: 489.—(M. Pinner)*

Syphilis of Lung.—Syphilis of the lung is not rare among the Bantus of South Africa. The lesions belong to the tertiary stage and consist of gummata or diffuse fibrosis or combinations of each. The middle and lower lobes are most often affected. Pulmonary lesions are almost always accompanied by syphilitic aortitis. The symptoms and signs simulate those of the more chronic pulmonary diseases. Roentgenographically there may be lobar or patchy infiltration, oval opacities of varying sizes, accentuation of the bronchial and vascular shadows or complete opacity of one side of the chest with retraction of the

mediastinum. The following criteria must be fulfilled for diagnosis: the condition must be chronic; the sputum must not contain tubercle bacilli; the serological test for syphilis must be positive; there must be radiological evidence of a pulmonary lesion; there must be a rapid clinical and roentgenological improvement on anti-syphilitic therapy. Four cases are described in detail.—*Syphilis of the Lung in Bantus, B. A. Dormer, J. Friedlander & F. J. Wiles, Brit. J. Tuberc., October, 1945, 39: 85.*—(*A. G. Cohen*)

Syphilis of Lung.—The rarity of syphilis of the lungs is unexplained. The difficulties encountered in establishing a scientifically irrefutable diagnosis, even on postmortem examination, account only partially for this rarity. Syphilitic lung disease may assume the characteristics of any type of pulmonary affection. Diagnosis of probability can be established in certain cases based on negative and positive data. Of relative importance for the diagnosis of syphilis is the fact that in spite of extensive pulmonary lesions, the general condition remains good. There are no roentgenological findings typical for syphilis. Its diffusion along the bronchovascular tree on the one hand and the gummous, process in the lung parenchyma on the other account for the polymorphous X-ray findings in pulmonary syphilis. The examination of the sputum for treponema is dissappointing and animal inoculation is a cumbrous process. The diagnosis becomes even more difficult when syphilis is associated with other pulmonary processes, such as tuberculosis or fungus disease. It is important to establish whether the subject having a pulmonary involvement is syphilitic. This is, however, not always easy or it may be impossible. In the presence of pulmonary disease of unexplained etiology in a syphilitic individual, antiluetic treatment should be undertaken. A careful evaluation of the results of such therapy will, in many cases, corroborate the suspected diagnosis. Based on the above mentioned criteria, diagnosis of pulmonary syphilis was tentatively made in 4 cases.—*Sifilis pleuropulmonar, R. E. M. Pittaluga, Hoja tisiol, September, 1945, 5: 330.*—(*L. Molnar*)

Pulmonary Mycosis.—The signs and symptoms caused by pulmonary mycosis are very much like those caused by pulmonary tuberculosis. The X-ray appearance of the lesions may also simulate closely that found in tuberculosis. This explains the frequent diagnostic error, which may cost the patient long periods of hospitalization before the diagnosis is corrected. Hemoptysis is a frequent symptom in mycotic diseases of the lung. In 3 cases observed by the authors, hemoptysis was a prominent symptom. The diagnosis of mycosis can be established only by careful evaluation of the laboratory methods for the demonstration of fungi in the sputum or in the gastric contents. In 2 cases aspergillus was recovered from the sputum. Massive doses of iodine were effective in one of these cases, while they failed to cure the second patient. The third patient had actinomycosis, simulating a suppurative or gangrenous pulmonary lesion, which responded well to penicillin treatment.—*Micosis pulmonar, R. Ortuzar, R. Croxatto & M. Cruzat, Rev. méd. de Chile, January, 1946, 74: 27.*—(*L. Molnar*)

Fungus Diseases.—A survey was made of mycotic infections in England. Under the heading of mycoses of the lung, 4 important conditions are reported. Many specimens of sputum were examined from conditions suspected to be moniliasis of the lung, and from the greater number of these *Candida albicans* was cultivated. However, this organism is known to vegetate as a saprophyte or a harmless parasite in the throats of healthy persons and therefore its mere presence in the sputum is of uncertain diagnostic significance. In one case the fresh sputum contained masses of actively vegetating *Candida tropicales* intimately associated with pulmonary cells; the reported symptoms and physical signs and the X-ray picture were consistent with the accepted description of pulmonary moniliasis, and the disease yielded

quickly to treatment with potassium iodide. When mouth gargling and cleaning of the teeth were fastidiously carried out before expectoration into a sterilized receptacle in a control series of 32 patients suffering from pulmonary tuberculosis, in 68.75 per cent of them *Candida albicans* was more or less constantly present in the sputum before and after mouth-cleaning. It seems possible that in some of these cases the fungus may have been vegetating saprophytically in a lung cavity. In another group of patients with nontuberculous cavitation of the lung, on whom bronchoscopic swabbing was done, *Candida albicans*, although found in the sputum of some both before and after mouth-cleansing, was never found in the bronchoscopic swabbings. The potentially pathogenic mould *Aspergillus fumigatus* is found occasionally in samples of sputum from tuberculous patients with no known pathological significance. A culture identified as an unusually thermophilic strain of *A. fumigatus* was isolated from the sputum of a unique case of apparent acute aspergillosis of the lungs. Although the patient's state was critical, complete recovery was effected by administration of potassium iodide after sulphonamide therapy had failed. An interesting entity known as farmer's lung was reported. It is clinically and radiologically a fairly well characterized disease and is commonly believed to be a kind of pulmonary mycosis. The usual history is that a farmer, after working continuously for a time with mouldy hay from which a steam-like cloud of fungus-laden dust arises, develops a short dry cough with little or no expectoration; he may also suffer from general malaise, weakness and slight fever, but the outstanding feature is distressing dyspnea provoked by any physical exertion. Removal from exposure to mouldy hay dust is followed by rapid recovery, which is usually complete and permanent if further exposure is avoided. With successive seasonal recurrences the disease tends to progress to chronicity; the cough becomes more productive, the abundant sputum is tenacious and frothy or purulent and slight hemoptysis may occur; physical weakness is marked and the dyspnea severe. At this stage the lung may show fibrosis, emphysema, and possibly bronchiectasis, and the X-ray picture is usually characteristic. The relation of farmer's lung to inhalation of mouldy hay dust is unquestioned, but the commonly held view that it is a true pulmonary mycosis is based only on the occupational history of the patient and the cultivation of moulds from his sputum. The anaerobic species *Actinomyces bovis* was cultivated from the sputum in 2 cases. In one of these the lesion appeared to be confined to the lung, but in the other case the lung infection, complicated by empyema, was part of a generalized disease which proved to be fatal.—*A Survey of Fungous Diseases in Great Britain, J. T. Duncan, Brit. M. J., November 24, 1945, 2: 715.*—(*D. H. Cohen*)

Moniliasis.—In a 44 year old woman a diagnosis of pulmonary moniliasis was made on the basis of sputum and X-ray studies. *Candida albicans* was isolated from the sputum on numerous occasions. The patient was sensitive to iodines and gentian violet therapy caused an unfavorable reaction. A skin test with an autogenous vaccine of *Candida albicans* was negative. No agglutinins for the fungus could be found in the patient's serum. A skin test with an *anti-candida albicans* rabbit serum was strongly positive. Hypersensitivity to rabbit serum was excluded. The patient was treated with increasing doses of the immune rabbit serum. The desensitization series was repeated twice. Following the administration of the serum the patient made a dramatic recovery.—*Recovery from Pulmonary Moniliasis following Serum Therapy, J. S. Hiatt, Jr. & D. S. Martin, J. A. M. A., January 26, 1946, 130: 205.*—(*H. Abeles*)

Coccidioidin Tests.—The authors observed an apparent increase in cases of minimal tuberculosis in an Army General hospital which served the southwestern part of the United States. Intracutaneous tests, with both tuberculin and coccidioidin, were carried out on all persons with suspicious lung lesions. One or more coccidioidin tests were made on

372 patients; 125 of these were positive. One hundred selected cases with positive coccidioidin test and residual X-ray findings were chosen for this study. Coccidioidomycosis is caused by the fungus *Coccidioides immitis*. The organism is present in the soil of certain arid regions: parts of central and southern California, Arizona, New Mexico and West Texas. It has been isolated also from a number of wild rodents. The organism is diphasic. The infective form occurs in the soil and on culture media in the form of hyphae with chlamydospores. In animal tissue the organism occurs as a spherule with a doubly refractile wall. The spherules, which vary from 10 to 60 micra in diameter, mutiply by endosporulation. The organism enters the body through inhalation of infected dust or, rarely, through a break in the skin. Most infections are mild, self-limited and involve the lungs and associated mediastinal lymph nodes. Immunity develops and reinfection does not occur. Very rarely, the infection gains entrance into the blood stream from the lungs; all organs may be involved and the fatality rate is high. On the chest X-ray films, the initial lesion is a pneumonic area of variable size and location. Shortly thereafter, one or both hilar regions usually show evidence of lymph node enlargement. The pneumonic density regresses within a period of weeks or months. The initial lesion may be confused with a typical pneumonia. In the course of healing, the lesion may occasionally remain unchanged; annular densities or strand-like infiltrations may persist. Fifty-two of the 100 patients gave a history of pulmonary symptoms following entrance into the desert; symptoms were not characteristic. The importance of X-ray examination is emphasized by the fact that physical examination of the chest is negative in most cases. The coccidioidin skin test is a very reliable procedure. Skin sensitivity does not develop in response to the subcutaneous injection of coccidioidin. In 2 positive cases the test later became negative as the patients became desperately ill with disseminated disease. False transient positive blood Kahn and Wasserman reactions were noted in 5 seriously ill patients. The sedimentation rate is elevated during active stages of the disease. The fungus was isolated by sputum culture in 9 patients; all were seriously ill. The spherules were also seen in spinal fluid smear in one patient. A positive smear with negative culture is not considered definitely indicative of infection. Complement fixation and precipitins may be found in the blood, spinal fluid and chest fluid in the active stages of the disease. The X-ray findings can be grouped under five major types: (*1*) pneumonic infiltrations; (*2*) mediastinal lymphadenopathy; these changes are very common, may persist for months, may occur with no demonstrable parenchymal lesion and they may serve as a means of differentiation from reinfection tuberculosis; (*3*) discrete nodular densities which may occasionally calcify; (*4*) annular shadows with relatively thick walls; (*5*) upper lobe infiltrations. Four cases, in which the above X-ray findings were observed, came to autopsy.—*A Study of One Hundred Cases with a Positive Coccidioidin Skin Test, D. Clark & J. H. Gilmore, Ann. Int. Med., January, 1946, 24: 40.*—(*H. R. Nayer*)

Pulmonary Actinomycosis.—The term actinomycosis is applied to two groups of diseases of man and animals. In one group, an anaërobic organism, *Actinomyces bovis*, is found; in this type, the characteristic "sulphur granules" are observed in pus or tissues. The second group includes aërobic filamentous branching organisms without any radial arrangement and without granule formation; two type species are: *Actinomyces graminis* which is non-acid-fast and *Actinomyces asteroides* which is acid-fast. Proved cases of infection with *Actinomyces graminis* are rare. A low grade pathogenicity of this organism has been demonstrated for rabbits. The case history of a 16-year old boy is presented in whom *Actinomyces graminis* was identified in bronchial secretion, sputa and pleural fluid before death and in pleural fluid and multiple abscesses of the lung at autopsy. The illness began with fever, left chest pain and nonproductive cough. On admission, there were sparse physical signs over the left

chest. These increased subsequently and roentgenogram revealed extensive involvement of the left lung. Bronchoscopy disclosed an inflammatory lesion causing partial obstruction of the left upper lobe bronchus. Treatment with sulfonamide drugs, roentgen ray radiation, iodides and blood transfusion was ineffective. Clinical course was progressively downhill with increasing dyspnea, drenching sweats and a wracking cough. A loud pericardial friction rub was heard toward the end of the illness. During the last forty-eight hours of his illness, patient received 100,000 units of penicillin. He died approximately three months following onset of symptoms. Autopsy revealed actinomycosis of the left upper lobe with invasion of the pericardium, chronic myocarditis, and left empyema. *Actinomyces graminis* was demonstrated both before and after death by smears and cultural means.—*Pulmonary Actinomycosis Due to Actinomyces Graminis, J. P. Lynch & Rebecca A. Holt, Ann. Int. Med., July, 1945, 23: 91.*—(*H. R. Nayer*)

Pulmonary Actinomycosis and Penicillin.—Visceral actinomycosis, especially in the stage of sinus formation, represents a very difficult therapeutic problem. One case of far advanced pulmonary actinomycosis with fistulae was treated with penicillin. Improvement in the patient's condition was noted after the administration of 1,000,000 units of penicillin, which became more accentuated after 3,000,000 units; sinus closure occurred after 8,000,000 units. Continuing the treatment until a total dosage of 15,800,000 units was reached during a period of six months, a state of apparent cure was obtained with gain in weight, improvement in the- Xray appearance of the lesions and an approximately normal blood count; the sedimentation rate remained, however, elevated. After a four-week period of interruption of the treatment there was a relapse which responded promptly to the resumed administration of penicillin. Although the value of penicillin in the treatment of actinomycosis cannot be properly assessed as yet, it would appear from this case that intensive and prolonged treatment may be effective, especially in the earlier stages of the disease.—*Actinomicosis toraco-pleuro-pulmonar y penicilina, A. E. Baila & A. J. Macchi, Rev. Asoc. méd. argent., March, 1946, 60: 151.*—(*L. Molnar*)

Hydatid Cyst.—The method of inclusion of sputum and staining with Best's carmin permits the diagnosis of hydatid disease before the rupture of the cyst, at a time when no scolices or hooks can be found in the sputum. This method was instrumental in arriving at a correct diagnosis of echinococcosis in 13 cases. In 12 of these cases the diagnosis was confirmed by surgical intervention; while in one case the rupture of the cyst occurred shortly after the sputum had been collected for examination. The chitinous external layer of the hydatid cyst has a solid and resistant structure. When the adventitial reaction of the organ, which is the site of the disease, develops favorable conditions for infection, the products of the resulting inflammation disintegrate the outer layers of the chitinous membrane. In the case of the lung, or in other organs which have a natural canalicular outlet, the disintegrated fragments may be conveyed with the secretions to the exterior. This is the rationale on which Best's staining method is based. The adventitia represents the active reaction of the lung to the presence of the parasite. The virtual space between the adventitia and the chitinous membrane is soon converted into a real space as a consequence of the necrosis and of the inflammatory changes that take place in this area. Bronchogenic or hematogeneous infection occurs and leads to suppuration. Bronchi may also be involved in the process and the damage suffered by their wall may cause perforation and drainage of the purulent materal through the bronchial tree. This process is the anatomical substratum of the known "congestive episodes" in the course of hydatid disease of the lung. These episodes are characterized by fever, chest pain, increase in the amount of expectoration and hemoptysis. Roentgenologically there is an increase of the shadow of the cyst in the first phase, followed by the appearance

of a gaseous layer around the cyst after the perforation of the bronchus and the elimination of the purulent material. Careful and repeated sputum examinations at the moment when these phenomena take place will lead to the correct diagnosis. The material derived from the chitinous membrane of the hydatid cyst is stained red with Best's carmin. Another characteristic of this material is the presence of phagocytic cells arranged in palisades around the hydatid structures. It is by no means easy always to reach a definite diagnostic conclusion based on the histological appearance because, besides hydatid derivatives, there may be present many other granular or filamentous Best-positive elements in the sputum. The shape and size, as well as the position of these particles, if carefully evaluated, will usually reveal their origin from the hydatid cyst, but it is emphasized that the finding of Best-positive particles has only value as a presumptive evidence of hydatid disease.—*Diagnostico de quiste hidatico hialina (no roto) del pulmon mediante la inclusion de esputos, E. P. Lasnier & J. F. Cassinelli, An. Fac de med. de Montevideo, December, 1945, 30: 903.*—(*L. Molnar*)

Hydatid Cyst.—Hydatid disease is very common in some countries. The parasite, *Echinococcus granulosus*, is a tapeworm and lives in the intestinal canal of the dog and allied species. Its ova are passed in the feces; they are then ingested by the intermediate host, most often sheep, but also other animals, including man. Some of these hatch in the stomach, enter the portal circulation and are ferried to the liver. The majority lodge here, but others pass on to the lungs and other organs. The embryo then grows; the surrounding tissue is compressed to form a capsule and the whole lesion is called an hydatid cyst. Further evolution occurs within the cyst. Eventually scolices are formed; these are the heads of the future tapeworms. When the sheep dies, the contaminated viscera may be ingested by dogs. In man, infestation generally takes place by direct contact with dogs. The live ova are found in the fur of the animals and enter the gastrointestinal tract. Children and farmhands are particularly prone to infection. The opinion that the ova enter the lungs directly has not been substantiated. Multiple cysts are present in one-third of all patients suffering from the disease. As the cyst grows in the lungs, encroachment upon the blood vessels and bronchi results in local areas of emphysema, atelectasis, infarction and pneumonitis. The course of events is influenced also by the position of the cyst. Those near the hilum often erode a major bronchus early and are coughed up; 70 to 80 per cent are thus cured spontaneously. Others erode a large blood vessel with fatal results. Cysts in the periphery of the lung invade the pleura early. A sterile effusion, empyema or pneumothorax may ensue. Invasion of the mediastinum may result in emphysema or suppuration. Pressure upon the chest wall may result in atrophy of the bones. Multiple cysts in the lung are not uncommon. A variety of complications may befall a simple cyst. It may die without suppuration. The cyst may rupture into a bronchus in a variety of ways. The chief complications are residual pulmonary changes, infection and anaphylaxis, due to liberation of hydatid fluid. Suffocation due to impaction of the membranes in the larynx may occur. Daughter cysts are acquired by rupture of a primary cyst located in the right heart. Cysts in the upper part of the right lobe of the liver always extend toward the thorax. Such extension can result in a variety of pleuropulmonary complications; in such cases, bile is frequently found in the sputum. No biological test in use is entirely specific, except the detection of part of the cyst or its contents in the sputum. However the combined use of the complement-fixation test and Casoni intracutaneous test has resulted in great accuracy in diagnosis. The ordinary roentgenographic appearance of a simple cyst is a rounded shadow of uniform density and sharp outline. They are seldom completely circular and the outline is generally blurred in one or more places. If air should be insinuated between the adventitia and the laminated membrane, a slender crescent will be seen, which is

pathognomonic. Other unusual signs, less frequently seen, result from the rupture of the cyst. Calcium deposited in the adventitia is a valuable sign of hydatid disease. Medical and roentgen therapy are of no value. Simple peripheral cysts can be removed by enucleation. The authors propose lobectomy for the treatment of larger or complicated cysts. In 4 cases the results have been gratifying.—*Pulmonary Hydatid Disease, M. R. Barrett & D. Thomas, Brit. J. Tuberc., April–July, 1944, 38: 89.*—(*A. G. Cohen*)

Boeck's Sarcoidosis.—The elucidation of the clinical picture of sarcoidosis has developed slowly. The skin lesions were first described under various names and gradually other signs were uncovered and correlated. The consensus, at present, seems to be veering away from the belief that the tubercle bacillus is the etiological agent. Other views as to etiology are: (*1*) nonspecific tissue response evoked by various agents such as leprosy, syphilis, yaws, brucellosis, leishmania and lymphogranuloma venereum; (*2*) reticulo-endotheliosis comparable to Hodgkin's disease; (*3*) neoplasm. The average age of reported cases lies between 20 and 40 years. The histopathology is uniformly constant, consisting essentially of collections of epithelioid cells arranged in the form of miliary tubercles. Occasionally, one or more giant cells are found in the centre and more rarely in the periphery of the tubercle. The absence of inflammatory changes and caseation is characteristic. There is a marked tendency to fibrosis. A slight anemia and eosinophilia are usually present. The erythrocyte sedimentation rate is increased and the serum protein rises to levels of 9.0 to 9.6 g. per cent. A peripheral monocytosis may be found in the early stages. The tuberculin reaction becomes negative in those who have the disease in its later stages; this occurs even in those who may react positively in the early stages. The most frequent sites of involvement are the skin, lymph nodes, lungs, liver, spleen and bone marrow. The skin lesions, usually present on the nose, cheeks, ear lobes, fingers and toes, appear as reddish infiltrations with sharp borders, localized in the subcutaneous tissues. Other variations of the skin lesions include papular eruptions, telangiectatic soft areas and large serpiginous areas. The enlarged lymph nodes are smooth, discrete, freely movable and painless. The hilar nodes are frequently involved. In the lungs, the sarcoid tubercles are present frequently in the parenchyma proper. The miliary lesions may result in diminution of the pulmonary vascular bed with increased resistence to the flow from the right heart, resulting eventually in heart failure. Minimal pulmonary symptoms may accompany extensive X-ray involvement. Bone lesions have been found in up to 20 per cent of patients. Typical changes are seen mainly in the phalanges but long bones may be involved. Areas of bone disease may be accompanied by cyanosis and bluish red discoloration. Joint involvement is usually not painful. The medullary portion of the bone is mainly involved. Two types of bone changes are present: (*1*) multiple, circular punched out areas of rarefaction and reticulation; (*2*) general atrophy of the bones of the hands and feet. Lesions of the eyes and orbit are frequent. The anterior part of the uveal tract is most frequently involved. Association of eye lesions with parotid enlargement, accompanied by facial paralysis, forms the uveo-parotid syndrome. Although occurring more rarely, involvement of almost every organ in the body has been reported including the pituitary, brain, heart, pancreas, kidney, thyroid and testes. Diagnosis can be made positively only by examination of biopsy specimens.—*Pathology of Boeck's Sarcoid, C. T. Stone, Jr., New Orleans M. & S. J., February, 1946, 98: 369.*—(*H. R. Nayer*)

Liver Puncture in Sarcoidosis.—The diagnosis of sarcoidosis can often be suspected clinically, but if no enlargement of superficial lymph nodes is present and biopsy cannot be done, the diagnosis remains in doubt. In the author's hands, aspiration biopsy of the liver has been found an extremely useful diagnostic test. In 14 patients in whom the diagnosis of sarcoidosis was made on clinical grounds, liver biopsy by aspiration yielded positive

results in 11. Typical tuberculoid lesions were usually situated in the portal areas, but were also found in the parenchyma. In the 3 patients who showed normal aspirations, 2 were in a clinical phase which was definitely inactive. The other case had characteristic skin lesions which were biopsied. The chances, then, of making the diagnosis in an active case of sarcoidosis by liver biopsy are excellent. Liver biopsies were also done on 9 cases of active pulmonary tuberculosis. Aside from a mild form of atrophy in 3 cases, nothing unsual was found. Specifically, there were no epithelioid tubercles present.—*On Morbid Conditions of the Liver and the Diagnosis of the Disease of Besnier-Boeck-Schaumann, F. S. P. van Buchem, Acta med. Scandinav., March 30, 1946, 124: 168.*—(*H. Marcus*)

Typhoid and Salmonella Infections.—Pleural and pulmonary complications of typhoid fever, although unusual, have been described in the American and European literature. Bronchitis is very frequent and usually mild. Typhoid pneumonia may be bronchial or lobar in type. Pulmonary infarction may also occur. Abscess is the rarest pulmonary complication of typhoid fever. Pleurisy is almost always accompanied by a subjacent pneumonitis. The pleural fluid is usually sero-fibrinous or hemorrhagic, rarely purulent. Pleural effusions in typhoid fever are benign. The possibility of a concurrent tuberculous effusion must always be considered. Typhoid bacilli have been isolated from such effusions. The authors report 2 cases of typhoid fever with complicating pleural empyema; typhoid bacilli were isolated from the pus in both instances. Both patients required surgical treatment for the empyemata; one terminated fatally. A third patient developed a typhoid osteochondritis of a rib following a bout of typhoid fever; this was cured by surgical excision. The chest complications of salmonella infections are similar to those of typhoid fever. *S. paratyphi A* or *B* are the most frequent pathogens; *S. suipestifer* is occasionally found. The authors report one patient with a pleural empyema from which, on different occasions, *S. paratyphi B*, *S. typhi murium* and *S. cholerae suis* were isolated. Another patient was seen with a perichondral abscess from which *S. cholerae suis* was isolated; this patient was cured by surgical excision and radiotherapy.—*Some Unusual Thoracic Complications of Typhoid and Salmonella Infections, G. R. Minor & M. L. White, Jr., Ann. Int. Med., January, 1946, 24: 27.*—(*H. R. Nayer*)

Neuromuscular System of Lung.—The lung does not only follow passively the movements of the thoracic cage but has an active movement of its own synchronized with the thorax. Under certain circumstances, there are discrepancies in these two movements which then result in disease. Each segment has a neuromuscular system of its own. In the thoracoscope, normal segments surrounded by atelectatic lung tissue can be easily recognized. The normal parenchyma dilates during inspiration while atelectatic segments remain immobile. The depression of the visceral surface which is typical of atelectasis, augments during inspiration. Generally these atelectases are of long standing but on certain occasions, the sudden beginning of an atelectasis can be seen during thoracoscopy. These atelectases are the result of a reflex and can be produced in animal experiments by irritation of the normal pleura. There was no bronchial dislocation or obstruction which could have been the cause of the atelectasis. Monaldi has shown that the pericavitary wall is not formed by fibrous tissue which would be anatomically irriversible. The pericavitary reaction is due to an atelectasis of pulmonary parenchyma which can be aerated again and recuperate its normal functions. The concept that this atelectatic wall is produced by the endocavitary pressure is wrong. Positive pressure is found in a very small number of cavities and generally it does not exceed more than 4 or 5 cm. of water. This would be entirely insufficient to cause the atelectasis. A few days after a Monaldi operation the X-ray film shows a shadow in the cavity

which extends into the surrounding tissue. The same shadow appears after open drainage without aspiration. This is due to serous fluid in the interstices. The atelectatic lung is strongly vascularized and the drop in the intraälveolar pressure facilitates the extravasation of the fluid. The elevation of the hemidiaphragm and the frequent deviation of the trachea towards the affected side is due to a reduction in volume of the atelectatic region. The reflex of contraction of the muscles in the regional parenchyma has all the characteristics of other muscle reflexes. Mechanically provoked atelectasis, as during bronchoscopy or Monaldi operation, may occupy the entire lung. But the autonomy of the neuro-vegetative system of the pulmonary segments allows each segment to contract independently. The human lung is morphologically and embryologically a composition of multiple elementary lungs. As further proof that there is a separate neuro-vegetative system in the pulmonary segments the author has succeeded in producing localized atelectasis and changes in the endocavitary pressure by subcutaneous injection of small quantities of acetyl-choline. Splendid illustrations and diagrams accompany the paper.—*Ensenanzas proporcionadas por la toracoscopia y por el metodo de Monaldi, D. Xalabarder, Publ. del Inst. Antituberculoso "Francisco Moragas", Barcelona, 1945, 6: 65.* —(*W. Swienty*)

Pulmonary Segments.—The lung can be divided into 4 great areas of ventilation, the dorsal, the ventral, the external parabronchial and the internal parabronchial areas. The apical segment is either part of the dorsal or of the ventral area. A pulmonary segment can be defined as a part of the lung which is ventilated by a branch of a lobar bronchus. The superior lobe is so divided in superior dorsal, apical, superior ventral and external parabronchial segments; the middle lobe into the first inferior ventral and the medial external parabronchial segment; and the inferior lobe in 4 inferior dorsal zones, 3 inferior ventral zones, an external parabronchial and the cardiac zone. The left lung has exactly the same subdivisions with the only difference that the region which corresponds to the middle lobe on the right is not fed by a principal bronchus but by a branch from the bronchus of the upper lobe. Each segment forms an anatomical unit and is separated from the neighboring segment by a connective tissue wall in which the veins run to the hilum. It may form an independent or accessory lobe which then shows definite interlobar fissures. The most frequent accessory lobe is the left middle lobe. The cardiac segment forms the mediastino-diaphragmatic triangle. If seen in an X-ray film, this triangle has been interpreted often as mediastinal pleurisy. But it is now established that the picture of increased linear markings or haziness in this area corresponds to an infiltration or an atelectasis of the cardiac segment. The cardiac segment is an anatomical unit with functional and pathological independence. The cardiac bronchus is a special bronchus. It ventilates an independent cardiac lobe in all mammals with the exclusion of man. It has a special tendency to malformations, such as bronchiectasis. The direct continuation of the air current from the trachea through the bronchus favors local air-borne infections and location of foreign bodies. The apical segment is aired by a ramification of the superior lobe bronchus. It is the zone of most frequent localization of tuberculosis. In the X-ray film it extends from the upper pole of the apex to the lower delimitation of the first intercostal space. Towards the midline, it blends into the hilum. The apical segment includes the apical, the infraclavicular and the intercleido-hilar zones. It is separated from the neighboring zones by a connective tissue wall. The typical "early infiltrate" is generally situated in the lateral portion of the infraclavicular region. The study of the reaction of the pulmonary segments towards tuberculosis, neoplasms, bronchiectasis, etc. helps in the diagnosis of inexplicable X-ray findings. The article is illustrated by excellent X-ray pictures and diagrams.—*Anatomia y fisiopatologia de las zonas pulmonares, I. Blajot Pena, Publ. del Inst. Antituberculoso "Francisco Moragas", Barcelona, 1945, 6: 35.*— (*W. Swienty*)